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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,540	03/08/2001	Adrian Bot	A30571-A-PCT/USA-A	7183

7590 01/07/2009

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EXAMINER	
SGAGIAS, MAGDALENE K	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
01/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/801,540	BOT ET AL.	
	Examiner	Art Unit	
	MAGDALENE K. SGAGIAS	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2008*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/24/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/18/08 has been entered.

Applicant's arguments filed 12/18/08 have been fully considered. Claims 1-2 are pending and under consideration. Claim 3 has been canceled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 rejection under 35 U.S.C. 103(a) as being unpatentable over Assateerawatt et al, [Asian Pacific Journal of Allergy and Immunology, 11: 85-91, 1993 (IDS)] in view of Donnelly et al, [Journal of Immunological Methods, 176: 145-152, 1994 (IDS)] is withdrawn.

Claims 1-2 rejection under 35 U.S.C. 103(a) as being unpatentable over Assateerawatt et al, (Asian Pacific Journal of Allergy and Immunology, 11: 85-91, 1993 (IDS)) in view of Donnelly et al, (Journal of Immunological Methods, 176: 145-152, 1994 (IDS)) and further in view of Chisari et al, (Springer Semin Immunopathol, 17: 261-282, 1995) is withdrawn.

Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Meheus et al,** [postgraduate Medical Journal, 63(Supp 2): 139-141, 1987 (IDS)] in view of **Whalen et al,** (Ann NY Acad Sci, 772:64-76, 1995); **Schirmbeck et al,** (Journal of Virology, 69(10): 5929–5934, 1995).

Meheus teaches infants of HBsAg-positive mothers (Group I) as well as those born to women without HBV markers (Group II) were vaccinated with a 10 micrograms dose of a recombinant DNA hepatitis B vaccine within 24 hours after birth according to a 0, 1, and 2 month schedule, with a booster dose planned 12 months later (abstract). Vaccination results in 14 (Group I) and 47 (Group II) neonates showed that at two months after the third dose of vaccine, 86% (6/7) and 100% (37/37), respectively, seroconverted, with anti-HBs geometric mean titres of 80 IU/l and 266 IU/l in the respective groups (abstract). No adverse reactions to the vaccine were observed. Meheus suggests the recombinant DNA hepatitis B vaccine is safe and highly immunogenic in newborns (abstract). Meheus et al, differ from the present invention for not teaching a naked recombinant nucleic acid encoding a relevant epitope to the target HBsAg epitopes.

However, at the time of the present invention **Whalen et al,** teach the use of plasmid vectors expressing the HBsAg, along with improved protocols for transfection of muscle fibers and methods with which to investigate the characteristics of the strong immune response given by this antigen after DNA-mediated immunization (abstract). Whalen teaches HBsAg-bearing particles are formed such that the B and T epitopes are presented to the immune system in a way resembling that of the natural viral or subviral particles. Whalen teaches DNA-mediated immunization with the HBsAg-expressing plasmid vectors induces strong CTL responses as well as a dominant Th1 phenotype among the splenic lymphocytes of immunized mice. The Th1 cytokine profile can be obtained in two different strains of mice and with two types of

proteins, HBsAg and beta-galactosidase. Whalen teaches small amounts of protein produced by DNA-mediated immunization (on the order of nanograms) are capable of inducing strong immune responses at the level of B and T cells. **Schirmbeck et al,** supplements the teachings of Whalen by teaching mice immunized either by injection of a low dose of recombinant HBsAg protein preparations, by infection with recombinant vaccinia virus carrying an HBsAg-encoding gene, or by **intramuscular transfer of plasmid DNA encoding HBsAg epitopes** under appropriate promoter control the most potent priming of class I-restricted CTL to HBsAg in vivo was observed with DNA immunization and both Kb- and Db-restricted CTL reactivity to HBsAg emerged in *H-2b* mice (abstract). Schirmbeck teaches the Ld-restricted S28-39 epitope a CTL epitope of HBsAg detectable in *H-2d* BALB/c mice (Table 1 and p 5933, 1st column). Schirmbeck suggests nucleic acid immunization not only is extremely efficient but also reveals an extended spectrum of potentially immunogenic epitopes of protein antigens (abstract). Nucleic acid immunization represents a simple and efficient technique to prime class I-restricted T cells (abstract). DNA immunization can define an extended spectrum of potentially immunogenic epitopes of protein antigens that are not revealed by alternative vaccination protocols. Schirmbeck suggests that nucleic acid immunization can be used effectively to define the immunogenicity of a protein antigen for class I-restricted T cells in vivo. Because of the efficiency of CTL induction by DNA immunization, this type of antigen delivery will be of interest not only for prevention but also for therapeutic vaccine strategies in which induction or boosting of specific CTL reactivity in chronically infected patients is the aim. Schirmbeck suggests obvious candidates are vaccines designed to combat persistent viral infections of chronic hepatitis B and C (abstract). As such, Whalen taken with Schirmbeck provide sufficient motivation for one ordinary skill in the art to apply the plasmid DNA hepatitis B virus surface antigen (HBsAg) epitopes vaccine of Schirmbeck in the neonates of Meheus et al.

Accordingly, in view of the teachings of Whalen taken with Schirmbeck et al, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to apply plasmid DNA hepatitis B virus surface antigen (HBsAg) vaccine in neonates at birth or 1 month of high risk neonates born from HBsAg positive mothers with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make such a modification as Schirmbeck suggests that nucleic acid immunization can be used effectively to define the immunogenicity of a protein antigen for class I-restricted T cells in vivo and particularly because of the efficiency of CTL induction by DNA immunization, this type of antigen delivery will be of interest not only for prevention but also for therapeutic vaccine strategies in which induction or boosting of specific CTL reactivity in chronically infected to combat persistent viral infections of chronic hepatitis B and C.

Meheus taken with Whalen taken with Schirmbeck provide teaching, suggestion, and motivation to perform the instantly claimed methods.

The instant claims combine the elements of plasmid DNA hepatitis B virus surface antigen (HBsAg) vaccine in neonates, which taught in Meheus taken with Whalen taken with Schirmbeck. This general method has been shown to be used successfully with the Ld-restricted S28-39 epitope a CTL epitope of HBsAg detectable in *H-2d* BALB/c mice, as expected and predictable function in the instantly claimed methods.

Supreme Court reaffirmed principles based on its precedent that "[t]he combination of Familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR International Co. v. Teleflex Inc. (KSR), 550 U.S. at, 82 USPQ2d at 1395. Therefore, in view of Meheus taken with Whalen taken with Schirmbeck it would be *prima facie* obvious for one of skill in the art to apply the plasmid DNA hepatitis B virus surface antigen (HBsAg) epitopes vaccine in neonates.

Thus, the claimed invention as a whole, is clearly prima facie obvious in the absence of evidence to the contrary.

Applicant's arguments are moot in lieu of new rejections.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571) 272-3305. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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/Peter Paras, Jr./
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